

REMARKS

Claims 1 and 3-29 are pending in this application for the Examiner's review and consideration.

Claim Rejections – 35 USC § 103

Claims 1, 3-7, 9-21 and 23-29 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over US Patent Application Publication No. 2003/0208152 to Avrahami et al. (referred to hereinafter as "Avrahami") in view of US Patent No. 7,505,812 to Eggers et al. (referred to hereinafter as "Eggers").

The Office Action alleges that Avrahami discloses the method as claimed but acknowledges that it does not disclose generating a second plurality of micro-channels in the same area of skin to facilitate transdermal delivery of the carrier. The Office Action further alleges that Eggers discloses an electrosurgical system to open or maintain patency of openings that is also used for ablating the stratum corneum, and concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the usage of the device of Avrahami to also apply its electrical field after initially ablating tissue as suggested by Eggers in order to maintain the patency of the newly created channels.

Applicant respectfully disagrees. As indicated in the Amendment filed on November 30, 2010, Avrahami teaches methods of transdermal delivery of a substance wherein micro-channel generation is performed prior to the delivery of the substance (see, e.g., p. 8, penultimate line through p. 9, first line of the November 30, 2010 Amendment). Eggers does not remedy the deficiencies of Avrahami. Eggers discloses methods for maintaining patency in hollow body passages which become partially or totally occluded by invasive cellular growth or invasive solid tumor growth, suitable hollow body passages include ducts, orifices, lumens, and particularly coronary arteries (see, e.g., Eggers at col. 2, line 64 through col. 3, line 5). Eggers further teaches an apparatus for maintaining patency of the hollow body passages which comprises a catheter system comprising an electrosurgical catheter which comprises an elongate, flexible shaft body including a tissue ablating region where one or more active electrodes and a return electrode are present (*id.* at col. 9, lines 20-50). According to Eggers, the method comprises advancing the electrosurgical catheter within the body passage such that an electrode terminal is positioned near the occlusive media. High frequency voltage is applied to one or more electrode

terminals at the distal end of the catheter such that an electrical current flows from the electrode terminals, through the region of the occlusive media and to the return electrode to selectively remove the occlusive media. As a result, the vessel is recanalized (*id.* at col. 3, lines 17-28). Thus, Eggers discloses a method for maintaining patency in existing internal body passages which are subject to occlusion by invasive growth. Eggers neither discloses nor suggests generating new micro-channels in the stratum corneum for facilitating transdermal delivery of an active agent, specifically an oligonucleotide or polynucleotide, as presently claimed.

Thus, contrary to the Office Action's assertion, one of ordinary skill in the art would not be motivated to combine Avrahami and Eggers so as "to modify the usage of the device of Avrahami to also apply its electrical field after initially ablating tissue as suggested by Eggers in order to maintain the patency of the newly created channels" (see page 3, 2nd paragraph of the pending Office Action, *emphasis added*). It should be noted that the presently claimed method for intradermal or transdermal delivery of an oligonucleotide or polynucleotide as recited in claim 1 comprises generating a first plurality of micro-channels, then applying to the area where the first plurality of micro-channels are present a pharmaceutical composition comprising an oligonucleotide or polynucleotide, and then generating a second plurality of micro-channels. Eggers simply has nothing at all to do with forming micro-channels of any type.

In contrast, nowhere in the current application is it disclosed that generating the second plurality of micro-channels is aimed at maintaining the patency of the first plurality of micro-channels. There also is no disclosure of opening a blocked or occluded body passage or opening. In the presently claimed method, the step of generating the second plurality of micro-channels is aimed at facilitating the transdermal delivery of the oligonucleotide or polynucleotide (see, e.g., the published application US 20080114281 at paragraph [0012]). This is even further emphasized when referring to the method for intradermal or transdermal delivery of an oligonucleotide or polynucleotide as recited in claim 16 which comprises applying to an area of the skin of a subject a pharmaceutical composition comprising an oligonucleotide or polynucleotide and then generating a plurality of micro-channels in the area of the skin after applying the composition. The method recited in claim 16 comprises generating new micro-channels and as such it does not and cannot "maintain the patency of the newly created channels". Thus, claims 1 and 16 are not obvious over Avrahami in view of Eggers, and the rejection of these claims under 35 U.S.C. 103(a) over Avrahami in view of Eggers should be

withdrawn. As claims 3-7 and 9-15 depend from claim 1 and include further recitations thereto and as claims 17-21 and 23-29 depend from claim 16 and include further recitations thereto, these claims are also not obvious over Avrahami in view of Eggers, and the rejection of these claims should be withdrawn as well.

Claims 8 and 22 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Avrahami and Eggers as applied to claim 1, and further in view of US Patent No. 6,429,200 to Monahan et al. (referred to hereinafter as "Monahan"). The Office Action asserts that while Avrahami substantially discloses the apparatus as claimed, it does not disclose additives to the active agent such as lipids, polycations or nuclease inhibitors. The Office Action further asserts that Monahan discloses adding polycations to polynucleotides and reverse micelles in order to compact the polynucleotides. The Office Action thus concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the delivery device/method of Avrahami to utilize polycations and reverse micelles as taught by Monahan to compact the polynucleotides for gene delivery purposes.

Applicant respectfully disagrees. As indicated above, the combination of Avrahami and Eggers does not disclose or suggest a method for intradermal or transdermal delivery of an oligonucleotide or polynucleotide by generating micro-channels in the skin after application of a composition that contains an oligonucleotide or polynucleotide, as presently claimed. Eggers discloses a device that is different from that of Avrahami and one which does not create micro-channels. Furthermore, Eggers' device removes occluded material and does not deliver oligonucleotides or polynucleotides. Monahan does not remedy the deficiencies of Avrahami and Eggers. Monahan discloses a process for delivering a complex to a cell comprising inserting a nucleic acid into a reverse micelle (see, e.g., Monahan at col. 5, lines 55-63). According to Monahan, compounds can be added to the nucleic acid/micelle mixture. Among the compounds, polymers such as polyions (polycations, polyamines, and polyanions) are listed (*id.* at col. 5, line 67 through col. 6, line 6). Like Eggers, Monahan does not disclose or suggest generating micro-channels after the application of the composition, as presently claimed. Thus, even if one of ordinary skill in the art combines the teachings of Avrahami, Eggers and Monahan, he would not obtain the methods of intradermal or transdermal delivery of an oligonucleotide or polynucleotide as recited in claims 8 and 22, which add further features to claims 1 and 16, respectively. Therefore, the rejection of claims 8 and 22 should be withdrawn.

In view of the above, it is respectfully submitted that all current rejections have been overcome and should be withdrawn. Accordingly, the entire application is believed to be in condition for allowance, early notice of which would be appreciated. Should the Examiner not agree, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of this application.

Date: June 27, 2011

Respectfully submitted,

A handwritten signature in cursive script, reading "Allan A. Fanucci". The signature is written in dark ink and is positioned above a horizontal line.

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